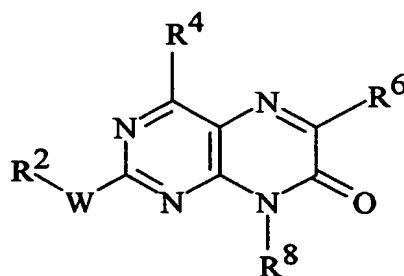


-88-

CLAIMS

What is claimed is:

1. A compound of the formula



5/4
257
258

- 5 and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof, wherein:

W is NH, S, SO, or SO₂;

R² is:

C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl,

- 10 (CH₂)_n-aryl, COR⁴, (CH₂)_n-heteroaryl, and (CH₂)_n-heterocyclyl, wherein each of the foregoing alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl groups can be unsubstituted or substituted with from 1 to 5 substituent groups selected from:

- 15 (a) halogen
(b) amino, alkylamino, and dialkylamino
(c) alkoxy, aminoalkoxy, alkylaminoalkoxy, and dialkylaminoalkoxy
(d) phenyl, substituted phenyl, phenoxy, and substituted phenoxy
(e) hydroxy
20 (f) thio, alkylthio
(g) cyano
(h) nitro
(i) alkanoyl, aminoalkanoyl, alkylaminoalkanoyl, and dialkylaminoalkanoyl

-89-

- (j) aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl
- (k) amino-C₃-C₇ cycloalkylcarbonyl, alkylamino-C₃-C₇ cycloalkylcarbonyl, and dialkylamino-C₃-C₇ cycloalkylcarbonyl
- (l) COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z, where Z is hydrogen, hydroxy, alkoxy, SOZ, lower alkyl, substituted alkyl, amino, alkylamino, dialkylamino, piperidinyl, substituted piperidinyl, morpholinyl, substituted morpholinyl, piperazinyl, and substituted piperazinyl
- (m) a carbocyclic group containing from 3 to 7 ring members, one or two of which may be a heteroatom selected from O or N, and wherein the carbocyclic group may be substituted with one, two, or three substituent groups selected from:
- (1) halogen
 - (2) hydroxy
 - (3) alkyl, aminoalkyl, alkyl and dialkylaminoalkyl
 - (4) trifluoromethyl
 - (5) alkoxy
 - (6) amino, alkylamino, dialkylamino, alkanoylamino
 - (7) COZ, CO₂Z, SOZ, SO₂Z, or PO₃Z
 - (8) aryl
 - (9) heteroaryl
 - (10) (CH₂)_n morpholino
 - (11) (CH₂)_n piperazinyl
 - (12) (CH₂)_n piperidinyl
 - (13) (CH₂)_n tetrazolyl
- (n) trifluoromethyl;

R⁴ and R⁶ are:

- (a) the same or different and are independently hydrogen, halogen, lower alkyl, or lower alkoxy, substituted alkyl, (CH₂)_n-alkenyl, (CH₂)_n-

-90-

alkynyl, $(\text{CH}_2)_n$ -cyano, amino, aminoalkoxy, phenoxy, hydroxy, trifluoromethyl, mono- or dialkylamino, mono- or dialkylaminoalkoxy, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, SO_2Z , PO_3Z , COZ , CO_2Z , SOZ , aminoalkanoyl, aminocarbonyl, amino- C_3 - C_7 -cycloalkylcarbonyl, and N-mono- or N,N-dialkylaminocarbonyl;

(b) the same or different and are independently $(\text{CH}_2)_n$ -aryl, $(\text{CH}_2)_n$ -heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl and heteroaryl is unsubstituted or substituted with up to five groups selected from halogen, hydroxy, lower alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamide, SO_3Z , and PO_3Z ;

R^8 is:

(a) hydrogen, lower alkyl, substituted alkyl, $(\text{CH}_2)_n$ -alkenyl, substituted alkenyl, $(\text{CH}_2)_n$ -alkynyl, substituted alkynyl, or a $(\text{CH}_2)_n$ -carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups selected from the group consisting of halogen, hydroxy, lower alkyl, lower alkoxy, acetoxy, amino, COZ , CO_2Z , SOZ , SO_2Z , PO_3Z , mono- or dialkylamino, aryl and heteroaryl;

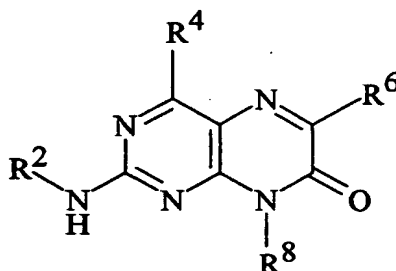
(b) $(\text{CH}_2)_n$ -aryl, $(\text{CH}_2)_n$ -heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl or heteroaryl is unsubstituted or substituted with up to five groups selected from the group consisting of halogen, hydroxy, lower alkyl, substituted alkyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, thiol, thioalkyl, nitrile, nitro,

-91-

carboxylic acid, carboxylic acid esters, carboxamides, COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z; and

n is an integer from 0 to 6, and provided that R⁸ is other than hydrogen or C₁-C₃ alkyl when R² is methyl, ethyl, or acetyl.

5 2. A compound of the formula



and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof, wherein:

R² is:

- 10 C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, (CH₂)_n-aryl, COR⁴, (CH₂)_n-heteroaryl, and (CH₂)_n-heterocyclyl, wherein each of the foregoing alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl groups can be unsubstituted or substituted with from 1 to 5 substituent groups selected from:
- 15 (a) halogen
- (b) amino, alkylamino, and dialkylamino
- (c) alkoxy, aminoalkoxy, alkylaminoalkoxy, and dialkylaminoalkoxy
- (d) phenyl, substituted phenyl, phenoxy, and substituted phenoxy
- 20 (e) hydroxy
- (f) thio, alkylthio
- (g) cyano
- (h) nitro
- 25 (i) alkanoyl, aminoalkanoyl, alkylaminoalkanoyl, and dialkylaminoalkanoyl

-92-

- (j) aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl
- (k) amino-C₃-C₇ cycloalkylcarbonyl, alkylamino-C₃-C₇ cycloalkylcarbonyl, and dialkylamino-C₃-C₇ cycloalkylcarbonyl
- (l) COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z, where Z is hydrogen, hydroxy, alkoxy, lower alkyl, substituted alkyl, amino, alkylamino, dialkylamino, piperidiny, substituted piperidiny, morpholiny, substituted morpholiny, piperaziny, and substituted piperaziny
- (m) a carbocyclic group containing from 3 to 7 ring members, one or two of which may be a heteroatom selected from O or N, and wherein the carbocyclic group may be substituted with one, two, or three substituent groups selected from:
- (1) halogen
 - (2) hydroxy
 - (3) alkyl, aminoalkyl, alkyl and dialkylaminoalkyl
 - (4) trifluoromethyl
 - (5) alkoxy
 - (6) amino, alkylamino, dialkylamino, alkanoylamino
 - (7) COZ, CO₂Z, SOZ, SO₂Z, or PO₃Z
 - (8) aryl
 - (9) heteroaryl
 - (10) (CH₂)_n morpholino
 - (11) (CH₂)_n piperaziny
 - (12) (CH₂)_n piperadiny
 - (13) (CH₂)_n tetrazoly
- (n) trifluoromethyl;

R⁴ and R⁶ are:

- (a) the same or different and are independently hydrogen, halogen, lower alkyl, or lower alkoxy, substituted alkyl, (CH₂)_n-alkenyl,

-93-

substituted alkenyl, $(\text{CH}_2)_n$ -alkynyl, substituted alkynyl, $(\text{CH}_2)_n$ -cyano, amino, aminoalkoxy, phenoxy, hydroxy, trifluoromethyl, mono- or dialkylamino, mono- or dialkylaminoalkoxy, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, SO_2Z , PO_3Z , COZ , CO_2Z , SOZ , aminoalkanoyl, aminocarbonyl, amino- C_3 - C_7 -cycloalkylcarbonyl, and N-mono- or N,N-dialkylaminocarbonyl;

(b) the same or different and are independently $(\text{CH}_2)_n$ -aryl, $(\text{CH}_2)_n$ -heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl and heteroaryl is unsubstituted or substituted with up to five groups selected from halogen, hydroxy, lower alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamide, SO_3Z , and PO_3Z ;

R^8 is:

(a) hydrogen, lower alkyl, substituted alkyl, $(\text{CH}_2)_n$ -alkenyl, substituted alkenyl, $(\text{CH}_2)_n$ -alkynyl, substituted alkynyl, or a $(\text{CH}_2)_n$ -carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups selected from the group consisting of halogen, hydroxy, lower alkyl, lower alkoxy, acetoxy, amines, carboxylic acids, carboxylic esters, carboxyamides, amino, COZ , CO_2Z , SOZ , SO_2Z , PO_3Z , mono- or dialkylamino, aryl and heteroaryl;

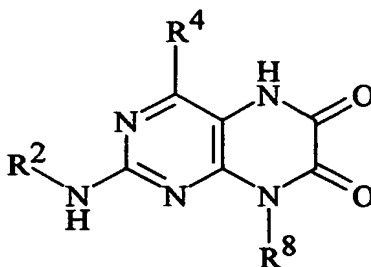
(b) $(\text{CH}_2)_n$ -aryl, $(\text{CH}_2)_n$ -heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl or heteroaryl is unsubstituted or substituted with up to five groups selected from the group consisting of halogen, hydroxy, lower alkyl, substituted alkyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, alkenyl, substituted

-94-

alkenyl, alkynyl, substituted alkynyl, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z; and

n is an integer from 0 to 6, and provided that R⁸ is other than hydrogen or C₁-C₃ alkyl when R² is methyl, ethyl, or acetyl.

3. A compound of the formula



and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof, wherein:

R² is:

C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl,

(CH₂)_n-aryl, COR⁴, (CH₂)_n-heteroaryl, and (CH₂)_n-heterocyclyl,

wherein each of the foregoing alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl groups can be unsubstituted or substituted with from 1 to 5 substituent groups selected from:

- (a) halogen
- (b) amino, alkylamino, and dialkylamino
- (c) alkoxy, aminoalkoxy, alkylaminoalkoxy, and dialkylaminoalkoxy
- (d) phenyl, substituted phenyl, phenoxy, and substituted phenoxy
- (e) hydroxy
- (f) thio, alkylthio
- (g) cyano
- (h) nitro
- (i) alkanoyl, aminoalkanoyl, alkylaminoalkanoyl, and dialkylaminoalkanoyl

-95-

- (j) aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl
- (k) amino-C₃-C₇ cycloalkylcarbonyl, alkylamino-C₃-C₇ cycloalkylcarbonyl, and dialkylamino-C₃-C₇ cycloalkylcarbonyl
- (l) COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z, where Z is hydrogen, hydroxy, alkoxy, lower alkyl, substituted alkyl, amino, alkylamino, dialkylamino, piperidinyl, substituted piperidinyl, morpholinyl, substituted morpholinyl, piperazinyl, and substituted piperazinyl
- (m) a carbocyclic group containing from 3 to 7 ring members, one or two of which may be a heteroatom selected from O or N, and wherein the carbocyclic group may be substituted with one, two, or three substituent groups selected from:
- (1) halogen
 - (2) hydroxy
 - (3) alkyl, aminoalkyl, alkyl and dialkylaminoalkyl
 - (4) trifluoromethyl
 - (5) alkoxy
 - (6) amino, alkylamino, dialkylamino, alkanoylamino
 - (7) COZ, CO₂Z, SOZ, SO₂Z, or PO₃Z
 - (8) aryl
 - (9) heteroaryl
 - (10) (CH₂)_n morpholino
 - (11) (CH₂)_n piperazinyl
 - (12) (CH₂)_n piperidinyl
 - (13) (CH₂)_n tetrazolyl
- (n) trifluoromethyl;

R⁴ is:

- (a) the same or different and are independently hydrogen, halogen, lower alkyl, or lower alkoxy, substituted alkyl, (CH₂)_n-alkenyl, (CH₂)_n-

-96-

alkynyl, $(\text{CH}_2)_n$ -cyano, amino, aminoalkoxy, phenoxy, hydroxy, trifluoromethyl, mono- or dialkylamino, mono- or dialkylaminoalkoxy, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, SO_2Z , PO_3Z , COZ , CO_2Z , SOZ , aminoalkanoyl, aminocarbonyl, amino- C_3 - C_7 -cycloalkylcarbonyl, and N-mono- or N,N-dialkylaminocarbonyl;

(b) the same or different and are independently $(\text{CH}_2)_n$ -aryl, $(\text{CH}_2)_n$ -heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl and heteroaryl is unsubstituted or substituted with up to five groups selected from halogen, hydroxy, lower alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamide, COZ , CO_2Z , SOZ , SO_2Z , and PO_3Z ;

R^8 is:

(a) hydrogen, lower alkyl, substituted alkyl, $(\text{CH}_2)_n$ -alkenyl, substituted alkenyl, $(\text{CH}_2)_n$ -alkynyl, substituted alkynyl, or a $(\text{CH}_2)_n$ -carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups selected from the group consisting of halogen, hydroxy, lower alkyl, lower alkoxy, acetoxy, amino, COZ , CO_2Z , SOZ , SO_2Z , PO_3Z , carboxylic acids, esters, amides, mono- or dialkylamino, aryl and heteroaryl;

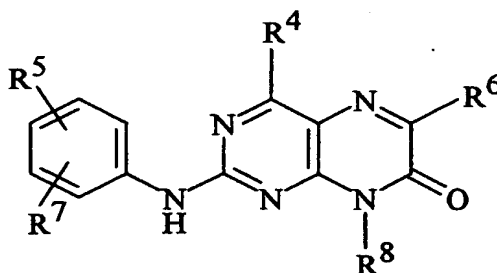
(b) $(\text{CH}_2)_n$ -aryl, $(\text{CH}_2)_n$ -heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl or heteroaryl is unsubstituted or substituted with up to five groups selected from the group consisting of halogen, hydroxy, lower alkyl, substituted alkyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, thiol, thioalkyl, nitrile, nitro,

-97-

carboxylic acid, carboxylic acid esters, carboxamides, COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z; and

n is an integer from 0 to 6, and provided that R⁸ is other than hydrogen or C₁-C₃ alkyl when R² is methyl, ethyl, or acetyl.

5 4. A compound of the formula



and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof, wherein:

R⁵ and R⁷ are the same or different and selected from:

- 10 (a) hydrogen, halogen, amino, aminoalkoxy, lower alkoxy, phenoxy, hydroxy, thiol, thioalkyl, nitrile, nitro, phenyl, substituted phenyl, heteroaryl, trifluoromethyl, mono- or dialkylamino, mono- or dialkylaminoalkoxy, alkanoylamino, aminocarbonyl, amino-C₃-C₇-cycloalkylcarbonyl, and N-mono- or
- 15 N,N-dialkylaminocarbonyl;
- (b) CO₂Z, COZ, SOZ, SO₂Z or PO₃Z, where Z is H, lower alkyl, hydroxy, alkoxy, substituted alkyl, amino, mono- or dialkylamino, piperidinyl, morpholinyl or piperazinyl (with or without substitution);
- 20 (c) lower alkyl unsubstituted or substituted with one or two groups selected from lower alkoxy, halogen, amino, hydroxy, mono- or dialkylamino, carboxylic acid, carboxamide, carboxylic acid ester, aryl or a carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and
- 25 nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups independently selected

-98-

from the group consisting of halogen, hydroxy, lower alkyl, lower alkoxy, amino, or mono- or dialkylamino;

- (d) a carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups independently selected from the group consisting of halogen, hydroxy, lower alkyl, branched alkyl, trifluoromethyl, lower alkoxy, amino, mono- or dialkylamino, aryl, heteroaryl, carboxylic acid, carboxamide, carboxylic acid ester, aryl, heteroaryl, morpholinoalkyl, piperazinylalkyl, piperadinylalkyl, tetrazolylalkyl, aminoalkyl and alkanoylamino;

R⁴ and R⁶ are:

- (a) the same or different and are independently hydrogen, halogen, lower alkyl, or lower alkoxy, substituted alkyl, (CH₂)_n-alkenyl, (CH₂)_n-alkynyl, (CH₂)_n-cyano, amino, aminoalkoxy, phenoxy, hydroxy, trifluoromethyl, mono- or dialkylamino, mono- or dialkylaminoalkoxy, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, SO₂Z, PO₃Z, COZ, CO₂Z, SOZ, aminoalkanoyl, aminocarbonyl, amino-C₃-C₇-cycloalkylcarbonyl, and N-mono- or N,N-dialkylaminocarbonyl;
- (b) the same or different and are independently (CH₂)_n-aryl, (CH₂)_n-heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl and heteroaryl is unsubstituted or substituted with up to five groups selected from halogen, hydroxy, lower alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamide, COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z;

R⁸ is:

- (a) hydrogen, lower alkyl, substituted alkyl, (CH₂)_n-alkenyl, substituted alkenyl, (CH₂)_n-alkynyl, substituted alkynyl, or a (CH₂)_n-

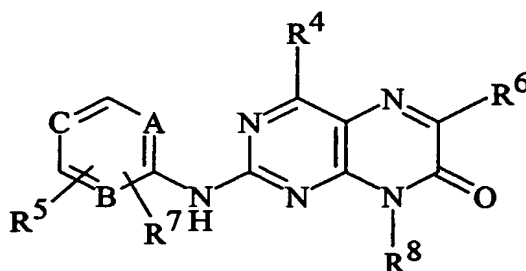
-99-

carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups selected from the group consisting of halogen, hydroxy, lower alkyl, lower alkoxy, acetoxy, amino, carboxylic acids, esters, amides, mono- or dialkylamino, aryl and heteroaryl;

(b) $(\text{CH}_2)_n$ -aryl, $(\text{CH}_2)_n$ -heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl or heteroaryl is unsubstituted or substituted with up to five groups selected from the group consisting of halogen, hydroxy, lower alkyl, substituted alkyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z; and

n is an integer from 0 to 6, and provided that R⁸ is other than hydrogen or C₁-C₃ alkyl when R² is methyl, ethyl, or acetyl.

5. A compound of the formula



and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof, wherein:

A, B, and C are the same or different and represent N or CH, provided that at least one of A, B, or C is CH;

R⁵ and R⁷ are the same or different and selected from:

-100-

- (a) hydrogen, halogen, amino, aminoalkoxy, lower alkoxy, hydroxy, trifluoromethyl, mono- or dialkylamino, mono- or dialkylaminoalkoxy, alkanoylamino, carbamoyl, amino-C₃-C₇-cycloalkylcarbonyl, N-mono- or N,N-dialkylcarbamoyl, or
- 5 (b) COZ, CO₂Z, SOZ, SO₂Z, PO₃Z, where Z is H, lower alkyl, hydroxy, alkoxy, amino, mono- or dialkylamino, piperidinyl, morpholinyl or piperazinyl, or
- (c) lower alkyl unsubstituted or substituted with one or two groups selected from lower alkoxy, halogen, amino, hydroxy, mono- or
- 10 dialkylamino, aryl or a carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups independently selected from the group consisting of halogen,
- 15 hydroxy, lower alkyl, lower alkoxy, amino, or mono- or dialkylamino, or
- (d) a carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with
- 20 one, two or three groups independently selected from the group consisting of halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, amino, mono- or dialkylamino, aryl, heteroaryl, morpholinoalkyl, piperazinylalkyl, piperidinylalkyl, tetrazolylalkyl, aminoalkyl and alkanoylamino;
- 25 R⁴ and R⁶ are the same or different and are selected from:
- (a) the same or different and are independently hydrogen, halogen, lower alkyl, or lower alkoxy, substituted alkyl, (CH₂)_n-alkenyl, (CH₂)_n-alkynyl, (CH₂)_n-cyano, amino, aminoalkoxy, phenoxy, hydroxy, trifluoromethyl, mono- or dialkylamino, mono- or
- 30 dialkylaminoalkoxy, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, SO₂Z, PO₃Z, COZ, CO₂Z,

-101-

SOZ, aminoalkanoyl, aminocarbonyl, amino-C₃-C₇-
cycloalkylcarbonyl, and N-mono- or N,N-dialkylaminocarbonyl;

(b) the same or different and are independently (CH₂)_n-aryl, (CH₂)_n-
heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl and
heteroaryl is unsubstituted or substituted with up to five groups
selected from halogen, hydroxy, lower alkyl, substituted alkyl,
alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, lower
alkoxy, amino, mono- or dialkylamino, trifluoromethyl, thiol,
thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters,
carboxamide, COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z;

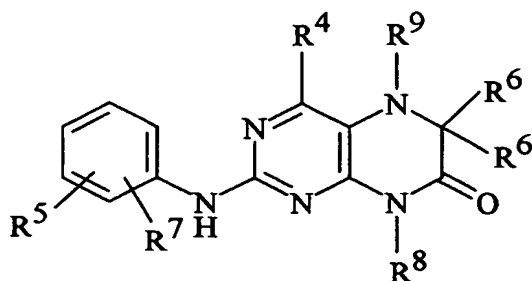
R⁸ is:

(a) hydrogen, lower alkyl, substituted alkyl, (CH₂)_n-alkenyl, substituted
alkenyl, (CH₂)_n-alkynyl, substituted alkynyl, or a (CH₂)_n-
carbocyclic group containing from 3-7 members, up to two of
which members are hetero atoms selected from oxygen and
nitrogen, wherein the carbocyclic group is unsubstituted or
substituted with one, two or three groups selected from the group
consisting of halogen, hydroxy, lower alkyl, lower alkoxy, acetoxy,
amino, carboxylic acids, esters, amides, mono- or dialkylamino,
aryl and heteroaryl;

(b) (CH₂)_n-aryl, (CH₂)_n-heteroaryl, arylalkyl, or heteroarylalkyl, wherein
each aryl or heteroaryl is unsubstituted or substituted with up to
five groups selected from the group consisting of halogen,
hydroxy, lower alkyl, substituted alkyl, lower alkoxy, amino,
mono- or dialkylamino, trifluoromethyl, alkenyl, substituted
alkenyl, alkynyl, substituted alkynyl, thiol, thioalkyl, nitrile, nitro,
carboxylic acid, carboxylic acid esters, carboxamides, COZ, CO₂Z,
SOZ, SO₂Z, and PO₃Z.

-102-

6. A compound of the formula



and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof, wherein:

5 R⁵ and R⁷ are the same or different and are selected from

- (a) hydrogen halogen, amino, aminoalkoxy, lower alkoxy, hydroxy, trifluoromethyl, mono- or dialkylamino, mono- or dialkylaminoalkoxy, alkanoylamino, carbamoyl, amino-C₃-C₇-cycloalkylcarbonyl, N-mono- or N,N-dialkylcarbamoyl, or
- 10 (b) CO₂Z, COZ, SOZ, SO₂Z, PO₃Z, where Z is hydrogen, lower alkyl, hydroxy, alkoxy, amino, mono- or dialkylamino, piperidinyl, morpholinyl or piperazinyl, or

- (c) lower alkyl unsubstituted or substituted with one or two groups selected from lower alkoxy, halogen, amino, hydroxy, mono- or
- 15 dialkylamino, aryl or a carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups independently selected from the group consisting of halogen,
- 20 hydroxy, lower alkyl, lower alkoxy, amino, or mono- or dialkylamino, or

- (d) a carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with
- 25 one, two or three groups independently selected from the group

-103-

consisting of halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, amino, mono- or dialkylamino, aryl, heteroaryl, morpholinoalkyl, piperazinyllalkyl, piperadinyllalkyl, tetrazolyllalkyl, aminoalkyl and alkanoylamino;

5 R^4 , R^6 , $R^{6'}$, and R^9 are:

(a) the same or different and are independently hydrogen, halogen, lower alkyl, or lower alkoxy, substituted alkyl, $(CH_2)_n$ -alkenyl, $(CH_2)_n$ -alkynyl, $(CH_2)_n$ -cyano, amino, aminoalkoxy, phenoxy, hydroxy, trifluoromethyl, mono- or dialkylamino, mono- or
10 dialkylaminoalkoxy, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, SO_2Z , PO_3Z , COZ , CO_2Z , SOZ , aminoalkanoyl, aminocarbonyl, amino- C_3 - C_7 -cycloalkylcarbonyl, and N-mono- or N,N-dialkylaminocarbonyl;

(b) the same or different and are independently $(CH_2)_n$ -aryl, $(CH_2)_n$ -
15 heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl and heteroaryl is unsubstituted or substituted with up to five groups selected from halogen, hydroxy, lower alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, thiol,
20 thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamide, COZ , CO_2Z , SOZ , SO_2Z , and PO_3Z ;

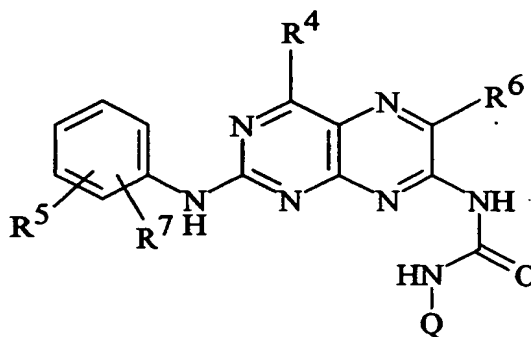
R^8 is:

(a) hydrogen, lower alkyl, substituted alkyl, $(CH_2)_n$ -alkenyl, substituted alkenyl, $(CH_2)_n$ -alkynyl, substituted alkynyl, or a $(CH_2)_n$ -
25 carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups selected from the group consisting of halogen, hydroxy, lower alkyl, lower alkoxy, acetoxy,
30 amino, carboxylic acids, esters, amides, mono- or dialkylamino, aryl and heteroaryl;

-104-

- (b) $(\text{CH}_2)_n$ -aryl, $(\text{CH}_2)_n$ -heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl or heteroaryl is unsubstituted or substituted with up to five groups selected from the group consisting of halogen, hydroxy, lower alkyl, substituted alkyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z.

7. A compound of the formula



and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof,
wherein:

R⁵ and R⁷ are the same or different and are selected from:

- (a) hydrogen, halogen, amino, aminoalkoxy, lower alkoxy, hydroxy, phenoxy, thiol, thiolalkyl, nitro, nitril, phenyl, substituted phenyl, heteroaryl, trifluoromethyl, mono- or dialkylamino, mono- or dialkylaminoalkoxy, alkanoylamino, carbamoyl, amino-C₃-C₇-cycloalkylcarbonyl, N-mono- or N,N-dialkylcarbamoyl, or
- (b) CO₂Z, COZ, SOZ, SO₂Z, PO₃Z, where Z is hydrogen, lower alkyl, substituted alkyl, amino, mono- or dialkylamino, piperidinyl, morpholinyl or piperazinyl (with or without substitution), or

-105-

- (c) lower alkyl unsubstituted or substituted with one or two groups selected from lower alkoxy, halogen, amino, hydroxy, mono- or dialkylamino, aryl or a carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups independently selected from the group consisting of halogen, hydroxy, lower alkyl, lower alkoxy, amino, or mono- or dialkylamino, or
- (d) a carbocyclic group containing from 3-7 members, up to two of which members are hetero atoms selected from oxygen and nitrogen, wherein the carbocyclic group is unsubstituted or substituted with one, two or three groups independently selected from the group consisting of halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, amino, mono- or dialkylamino, aryl, heteroaryl, morpholinoalkyl, piperazinylalkyl, piperadinyllalkyl, tetrazolylalkyl, aminoalkyl and alkanoylamino; and
- R^4 and R^6 are the same or different and are selected from:
- (a) the same or different and are independently hydrogen, halogen, lower alkyl, or lower alkoxy, substituted alkyl, $(CH_2)_n$ -alkenyl, $(CH_2)_n$ -alkynyl, $(CH_2)_n$ -cyano, amino, aminoalkoxy, phenoxy, hydroxy, trifluoromethyl, mono- or dialkylamino, mono- or dialkylaminoalkoxy, thiol, thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamides, SO_2Z , PO_3Z , COZ , CO_2Z , SOZ , aminoalkanoyl, aminocarbonyl, amino- C_3 - C_7 -cycloalkylcarbonyl, and N-mono- or N,N-dialkylaminocarbonyl;
- (b) the same or different and are independently $(CH_2)_n$ -aryl, $(CH_2)_n$ -heteroaryl, arylalkyl, or heteroarylalkyl, wherein each aryl and heteroaryl is unsubstituted or substituted with up to five groups selected from halogen, hydroxy, lower alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, lower alkoxy, amino, mono- or dialkylamino, trifluoromethyl, thiol,

-106-

thioalkyl, nitrile, nitro, carboxylic acid, carboxylic acid esters, carboxamide, COZ, CO₂Z, SOZ, SO₂Z, and PO₃Z; and

Q is hydrogen, lower alkyl, or substituted alkyl.

8. A compound which is selected from:

5 8-Methyl-2-[[4-(morpholin-4-yl)phenyl]amino]-6-phenyl-8H-pteridin-7-one;

 6-(2,6-Dichlorophenyl)-8-methyl-2-[[4-(morpholin-4-yl)phenyl]amino]-8H-pteridin-7-one;

10 6-(3,5-Dichloropyridin-4-yl)-8-methyl-2-[[4-(morpholin-4-yl)phenyl]amino]-8H-pteridin-7-one;

 6-(3,5-Dichloro-2,6-dimethoxypyridin-4-yl)-8-methyl-2-[[4-(morpholin-4-yl)phenyl]amino]-8H-pteridin-7-one;

 6-(3,5-Dibromopyridin-4-yl)-8-methyl-2-[[4-(morpholin-4-yl)phenyl]amino]-8H-pteridin-7-one;

15 2-[[4-[2-(Diethylamino)ethoxy]phenyl]amino]-8-methyl-6-phenyl-8H-pteridin-7-one;

 6-(2,6-Dichlorophenyl)-2-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-8-methyl-8H-pteridin-7-one;

20 6-(3,5-Dichloropyridin-4-yl)-8-methyl-2-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-8H-pteridin-7-one;

 6-(3,5-Dichloro-2,6-dimethoxypyridin-4-yl)-8-methyl-2-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-8H-pteridin-7-one;

 2-[[4-(Diethylaminocarbonyl)phenyl]amino]-8-methyl-6-phenyl-8H-pteridin-7-one;

25 6-(2,6-Dichlorophenyl)-2-[[4-(diethylaminocarbonyl)phenyl]amino]-8-methyl-8H-pteridin-7-one;

 6-(3,5-Dichloropyridin-4-yl)-2-[[4-(diethylaminocarbonyl)phenyl]amino]-8-methyl-8H-pteridin-7-one;

30 6-(3,5-Dichloro-2,6-dimethoxypyridin-4-yl)-2-[[4-(diethylaminocarbonyl)phenyl]amino]-8-methyl-8H-pteridin-7-one;

 8-Cyclopentyl-2-[[4-(morpholin-4-yl)phenyl]amino]-8H-pteridin-7-one;

-107-

8-Cyclopentyl-6-methyl-2-[[4-(morpholin-4-yl)phenyl]amino]-8H-pteridin-7-one;

8-Cyclopentyl-2-[[4-(4-methylpiperazin-1-yl)phenyl]amino]-8H-pteridin-7-one;

5 8-Cyclopentyl-6-methyl-2-[[4-(4-methylpiperazin-1-yl)phenyl]amino]-8H-pteridin-7-one;

8-Cyclopentyl-2-[(pyridin-4-yl)amino]-8H-pteridin-7-one;

2-[[4-(3-Aminopyrrolidin-1-yl)phenyl]amino]-8-cyclopentyl-8H-pteridin-7-one;

10 8-Cyclopentyl-2-[[4-(piperazin-1-yl)phenyl]amino]-8H-pteridin-7-one;

6-(3,5-Dimethoxyphenyl)-8-ethyl-2-[(pyridin-4-yl)amino]-8H-pteridin-7-one;

15 6-(3,5-Dimethoxyphenyl)-8-ethyl-2-[[4-[2-(diethylamino)ethoxy]phenyl]amino]-8H-pteridin-7-one;

2-[[4-[4-(*tert*-butoxycarbonyl)piperazin-1-yl]phenyl]amino]-8-cyclopentyl-8H-pteridin-7-one;

2-[[4-[3-(*tert*-butoxycarbonylamino)pyrrolidin-1-yl]phenyl]amino]-8-cyclopentyl-8H-pteridin-7-one;

20 8-Cyclopentyl-2-(4-fluoro-3-methyl-phenylamino)-8H-pteridin-7-one;

2-(3-Chloro-4-fluoro-phenylamino)-8-cyclopentyl-8H-pteridin-7-one;

25 8-Cyclohexyl-2-(4-fluoro-3-methyl-phenylamino)-8H-pteridin-7-one;

8-Cyclopentyl-2-{3-fluoro-4-[4-(3-morpholin-4-yl-propyl)piperidin-1-yl]-phenylamino}-8H-pteridin-7-one;

8-Cyclopentyl-2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pteridin-7-one;

30 8-Cyclopentyl-2-{4-[4-(3-piperazin-1-yl-propyl)-piperidin-1-yl]-phenylamino}-8H-pteridin-7-one;

8-Cyclopentyl-2-(4-{4-[3-(1H-tetrazol-5-yl)-propyl]-piperidin-1-yl}-phenylamino)-8H-pteridin-7-one;

-108-

8-Cyclopentyl-2-(4-fluoro-3-methyl-phenylamino)-6-methyl-8H-pteridin-7-one;

5-(8-Cyclopentyl-7-oxo-7,8-dihydro-pteridin-2-ylamino)-2-methyl-isoindole-1,3-dione;

5 N-[4-(8-Cyclopentyl-7-oxo-7,8-dihydro-pteridin-2-ylamino)-phenyl]-propionamide;

N-[4-(8-Cyclopentyl-6-methyl-7-oxo-7,8-dihydro-pteridin-2-ylamino)-phenyl]-propionamide;

10 2-(3-Chloro-4-piperazin-1-yl-phenylamino)-8-cyclopentyl-8H-pteridin-7-one;

2-[3-Chloro-4-(3-chloro-pyrrolidin-1-yl)-phenylamino]-8-cyclopentyl-8H-pteridin-7-one;

2-[3-Chloro-4-(3-chloro-4-trifluoromethyl-pyrrolidin-1-yl)-phenylamino]-8-cyclopentyl-8H-pteridin-7-one;

15 N-{1-[4-(8-Cyclopentyl-7-oxo-7,8-dihydro-pteridin-2-ylamino)-phenyl]-pyrrolidin-3-yl}-3,3-dimethyl-butyramide;

2-{4-[3-(1-Amino-1-methyl-ethyl)-pyrrolidin-1-yl]-3-chloro-phenylamino}-8-cyclopentyl-8H-pteridin-7-one;

20 2-[4-(3-Amino-cyclopentanecarbonyl)-phenylamino]-8-cyclopentyl-8H-pteridin-7-one;

8-Cyclopentyl-2-(4-methanesulfonyl-phenylamino)-6-methyl-8H-pteridin-7-one;

4-(8-Cyclopentyl-6-methyl-7-oxo-7,8-dihydro-pteridin-2-ylamino)-benzenesulfonamide;

25 8-Cyclopentyl-6-methyl-2-[4-(piperidine-1-sulfonyl)-phenylamino]-8H-pteridin-7-one;

6-(2,6-Dichloro-3-methoxyphenyl)-8-methyl-2-{[4-(morpholin-4-yl)phenyl]amino}-8H-pteridin-7-one; and

30 6-(2,6-Dichloro-3-hydroxyphenyl)-8-methyl-2-{[4-(morpholin-4-yl)phenyl]amino}-8H-pteridin-7-one.

9. A compound which is selected from:

-109-

8-Cyclopentyl-2-[[4-(morpholin-4-yl)phenyl]amino]-5*H*,8*H*-pteridine-6,7-dione; and

8-Cyclopentyl-2-[[4-(4-methylpiperazin-1-yl)phenyl]amino]-5*H*,8*H*-pteridine-6,7-dione;

5 8-Cyclopentyl-5-methyl-2-(4-piperazin-1-yl-phenylamino)-5,8-dihydro-6*H*-pteridin-7-one;

2-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-8-cyclopentyl-5-methyl-5,8-dihydro-6*H*-pteridin-7-one;

10 N-{1-[4-(8-Cyclopentyl-5-methyl-7-oxo-5,6,7,8-tetrahydropteridin-2-ylamino)-phenyl]-pyrrolidin-3-yl}-3,3-dimethyl-butyramide;

8-Cyclopentyl-5-methyl-2-(4-morpholin-4-yl-phenylamino)-5,8-dihydro-6*H*-pteridin-7-one;

8-cyclopentyl-2-{4-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-phenylamino}-5-methyl-5,8-dihydro-6*H*-pteridin-7-one;

15 8-cyclopentyl-2-{4-[4-(2-hydroxy-ethyl)-3,5-dimethyl-piperazin-1-yl]-phenylamino}-5-methyl-5,8-dihydro-6*H*-pteridin-7-one;

1-[4-(8-Isopropyl-5-methyl-7-oxo-5,6,7,8-tetrahydro-pteridin-2-ylamino)-phenyl]-pyrrolidine-3-carboxylic acid butylamide;

20 {4-[4-(8-Cyclopentyl-5-methyl-7-oxo-5,6,7,8-tetrahydro-pteridin-2-ylamino)-phenyl]-piperazin-1-yl}-acetic acid; and

6-(2,6-Dichloro-3-hydroxy-phenyl)-8-methyl-2-(4-morpholin-4-yl-phenylamino)-8*H*-pteridin-7-one.

10. A compound which is selected from:

25 1-tert-Butyl-3-[2-(4-fluoro-3-methyl-phenylamino)-pteridin-7-yl]-urea;

1-tert-Butyl-3-[2-(4-fluoro-3-methyl-phenylamino)-6-methyl-pteridin-7-yl]-urea;

1-tert-Butyl-3-(2-{4-[4-(3-morpholin-4-yl-propyl)-piperidin-1-yl]-phenylamino}-pteridin-7-yl)-urea;

30 1-tert-Butyl-3-(2-{4-[4-(3-piperazin-1-yl-propyl)-piperidin-1-yl]-phenylamino}-pteridin-7-yl)-urea; and

-110-

1-[2-(4-{4-[3-(3-Amino-pyrrolidin-1-yl)-propyl]-piperidin-1-yl}-phenylamino)-pteridin-7-yl]-3-tert-butyl-urea.

- 5 11. A pharmaceutical formulation comprising a compound of Claim 1 in combination with a pharmaceutically acceptable carrier, diluent, or excipient.
- 10 12. A method for controlling proliferative disorders in a mammal selected from the group consisting of cancer, psoriasis, vascular smooth muscle proliferation associated with a disorder selected from the group consisting of atherosclerosis, postsurgical vascular stenosis, and restenosis comprising administering to said mammal a therapeutically effective pharmaceutical formulation according to Claim 1.
13. A method of inhibiting a cyclin-dependent kinase comprising contacting the cyclin-dependent kinase with a compound selected from Claim 1.
14. A method of Claim 13 wherein said cyclin-dependent kinase is cdc2.
- 15 15. A method of Claim 13 wherein said cyclin-dependent kinase is cdk2.
16. A method of Claim 13 wherein said cyclin-dependent kinase is cdk4 or cdk6.
- 20 17. A method of inhibiting a growth factor-mediated tyrosine kinase comprising contacting said growth factor-mediated kinase with a compound selected from Claim 1.
18. A method of Claim 17 wherein said growth factor-mediated tyrosine kinase is platelet derived growth factor (PDGF).
19. A method of Claim 17 wherein said growth factor-mediated tyrosine kinase is fibroblast growth factor (FGF).

-111-

20. A method of treating a subject suffering from diseases caused by vascular smooth muscle cell proliferation comprising administration to said subject of a therapeutically effective amount of a compound selected from Claim 1.
- 5 21. A method of treating a subject suffering from cancer comprising administration to said subject of a therapeutically effective amount of a compound selected from Claims 1-10.
- 10 22. A method of treating a mammal suffering from cardiovascular diseases including atherosclerosis and restenosis; cancer; angiogenesis; viral infections including DNA viruses such as herpes and RNA viruses such as HIV; fungal infections; type 1 diabetes and diabetic neuropathy and retinopathy; multiple sclerosis; glomerulonephritis; neurodegenerative diseases including Alzheimer's disease; autoimmune diseases such as psoriasis, rheumatoid arthritis, lupus; organ transplant rejection and host versus graft disease; Gout; polycystic kidney disease; and inflammation including inflammatory bowel disease comprising administering a therapeutically effective amount of a compound selected from
- 15 Claims 1-10.